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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,725	06/21/2001	Jun Ueki	0760-0290P	3445

2292 7590 06/09/2003

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EXAMINER
KALLIS, RUSSELL

ART UNIT	PAPER NUMBER
1638	11

DATE MAILED: 06/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

FILE COPY

Office Action Summary	Application N .	Applicant(s)	
	09/856,725	UEKI ET AL.	
	Examiner	Art Unit	
	Russell Kallis	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-9 are pending and Claims 1-9 are examined.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant broadly claims a nucleic acid fragment of SEQ ID NO: 1 having one or more nucleotides substituted, deleted, inserted or added, or a part thereof; a nucleic acid fragment having not less than 70% sequence identity to SEQ ID NO: 1; and a nucleic acid fragment that hybridizes to SEQ ID NO: 1 under conditions of unspecified stringency wherein coding sequences downstream of said sequence show an increase in expression.

Applicant describes SEQ ID NO: 1 and 2.

Applicant does not describe a nucleic acid fragment of SEQ ID NO: 1 having one or more nucleotides substituted, deleted, inserted or added, or a part thereof; a nucleic acid fragment having not less than 70% sequence identity to SEQ ID NO: 1; or a nucleic acid fragment that hybridizes to SEQ ID NO: 1 under conditions of unspecified stringency wherein coding sequences downstream of said sequence show an increase in expression.

Given the claim breadth and lack of guidance as discussed above, the specification does not provide an adequate written description of the claimed invention.

See *University of California V. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

The court also addressed the manner by which genus of cDNAs might be described: "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." *Id.* At 1406.

Based upon the disclosure of SEQ ID NO: 1, there is insufficient relevant identifying characteristics to allow one skilled in the art to completely determine the structure of nucleic acid fragments or variants of SEQ ID NO: 1, other than SEQ ID NO: 1, that increase the expression of downstream coding sequences, including mutants and allelic variants, absent further guidance. Since the claimed genus encompasses undisclosed or yet to be discovered sequences that increase expression of downstream coding sequences, the disclosure of SEQ ID NO: 1 does not provide adequate description of the claimed genus. In view of the level of knowledge and skill in the art one skilled in the art would not recognize from Applicant's disclosure that Applicant was in possession of nucleic acid fragments or variants of SEQ ID NO: 1, other than SEQ ID NO: 1, that increase the expression of downstream coding sequences as broadly claimed.

Given the failure of a nucleic acid fragment of SEQ ID NO: 1 having one or more nucleotides substituted, deleted, inserted or added, or a part thereof; a nucleic acid fragment having not less than 70% sequence identity to SEQ ID NO: 1; or a nucleic acid fragment that hybridizes to SEQ ID NO: 1 under conditions of unspecified stringency to be adequately described wherein coding sequences downstream of said sequence show an increase in expression, methods of its use are also inadequately described. See Written Description Guidelines, Federal Register Vol. 66 No. 4, Friday January 5, 2001 "Notices", pages 1099-1111.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO: 1 and SEQ NID NO: 2, does not reasonably provide enablement for a nucleic acid fragment of SEQ ID NO: 1 having one or more nucleotides substituted, deleted, inserted or added, or a part thereof; a nucleic acid fragment having not less than 70% sequence identity to SEQ ID NO: 1; a nucleic acid fragment that hybridizes to SEQ ID NO: 1 under conditions of unspecified stringency. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Applicant broadly claims a nucleic acid fragment of SEQ ID NO: 1 having one or more nucleotides substituted, deleted, inserted or added, or a part thereof; a nucleic acid fragment having not less than 70% sequence identity to SEQ ID NO: 1; a nucleic acid fragment that hybridizes to SEQ ID NO: 1 under conditions of unspecified stringency wherein coding sequences downstream of said sequence show an increase in expression; and a method of promoting expression of a structural gene, and a plant thereof.

Applicant teaches SEQ ID NO: 1 (intron number 2 from the rice PLD gene genomic sequence); SEQ ID NO: 2 (intron number 2 from the rice PLD gene genomic sequence plus 37 nucleotides of exon at both ends); and SEQ ID NO: 2 having nearly 80 fold higher GUS activity when compared to the 35S enhancer/promoter in transformed maize.

Applicant does not teach any other nucleic acid sequence having nearly 80 fold greater GUS activity than the 35S promoter in transformed maize other than SEQ ID NO: 2 comprising SEQ ID NO: 1.

Isolating DNA fragments using stringent hybridization conditions, does not always select for DNA fragments whose contiguous nucleotide sequence is the same or nearly the same as the probe. Fourgoux-Nicol et al (1999, Plant Molecular Biology 40 :857-872) teach the isolation of a 674bp fragment using a 497bp probe incorporating stringent hybridization conditions comprising three consecutive 30 minute rinses in 2X, 1X and 0.1X SSC with 0.1% SDS at 65^0C (page 859, left column, 2^{nd} paragraph). Fourgoux-Nicol et al also teach that the probe and isolated DNA fragment exhibited a number of sequence differences comprising a 99bp insertion within the probe and a single nucleotide gap, while the DNA fragment contained 2 single nucleotide gaps and together the fragments contained 27 nucleotide mismatches. Taking into account the insertions, gaps and mismatches, the longest stretch of contiguous nucleotides to which the probe could hybridize consisted of 93bp of DNA (page 862, Figure 2).

The state of the art for modification of gene expression or of phenotypic characteristics in plants by genetic transformation is highly unpredictable. The specific effects of given promoters on gene expression in transformed plants of different species using a promoter comprising any number of non-exemplified combinations of elements or degrees of sequence identity can not be

anticipated with any reasonable degree of predictability and one of skill in the art must rely upon an empirical determination. Further, the expression patterns conferred by specific combinations of 35S-subdomains differed in tobacco and petunia indicating that a combination of cis-regulatory elements may be interpreted differently in different species. (Benfey *et al.*, Science 250:959-966, 1990, see Abstract, lines 14-18 and page 966 column 1, lines 29-45).

Non-coding nucleic acid sequences that exhibit base pair deletions, substitutions or rearrangements, cannot be expected to maintain their promoter or enhancer activity. Izawa T. *et al.* (J. Mol. Biol., 1993; Vol. 230; pp. 1131-1144) teach the nucleotides flanking the G-box (CACGTC) and C-box (GACGTC) hexameric cores were shown to affect protein binding activity and specificity of bZIP transcription factors (page 1132, bottom of right column; page 1134, bottom of left column).

Given the unpredictability in the art as to which substitutions, deletions, or additions to SEQ ID NO: 1 would be tolerated; the breadth of the claims encompassing a nucleic acid fragment of SEQ ID NO: 1 having one or more nucleotides substituted, deleted, inserted or added, or a part thereof; a nucleic acid fragment having not less than 70% sequence identity to SEQ ID NO: 1; a nucleic acid fragment that hybridizes to SEQ ID NO: 1 under conditions of unspecified stringency wherein coding sequences downstream of said sequence show an increase in expression in a transformed plant; the lack of guidance in the examples of the specification or in the prior art as to which deletions, substitutions, insertions or additions would best serve the invention or which fragments of the promoter of SEQ ID NO: 1 would best retain activity in a plant; although one of skill in the art can readily make nucleotide substitutions, additions, or deletions to a polynucleotide sequence one would not know based upon Applicant's disclosure

which embodiments would be inoperable and predictable eliminated, and thus undue trail and error experimentation would be needed by one skilled in the art to make and clone a multitude of non-exemplified variants of SEQ ID NO: 1 and would require one of skill in the art to test in a myriad of non-exemplified plants for enhanced expression of a polynucleotide coding sequence to alter the phenotype in a multitude of non-exemplified transformed plant species. Therefore, the invention is not enabled for the scope set forth in the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. All dependent claims are included in the rejection.

At Claim 1, lines 1-3, and throughout the claims, "the nucleotide sequence shown in SEQ ID NO: 1 in the Sequence Listing" is redundant. It is suggested "in the Sequence Listing" be deleted. All subsequent recitations of "in the Sequence Listing" are also rejected.

At Claim 1, line 4, "which has an activity to" is indefinite. It is unclear if it refers to SEQ ID NO: 1 or an altered SEQ ID NO: 1. Subsequent recitations of "which has an activity to" are also rejected.

At Claim 1, line 5, "gene" is indefinite. There is not a standard definition for this term, i.e., a gene can denote the coding region of an amino acid sequence or a gene can be defined as containing regulatory elements operably linked to the coding polynucleotide sequence encoding an amino acid sequence. If appropriate, the term "polynucleotide" can be used to denote nucleic acid molecules that encode a polypeptide. All subsequent recitations of "gene" are also rejected.

Further, "structural gene" does not indicate whether the promoter is operably linked to said "structural gene", i.e. included as a part of a promoter-structural gene construct or is only influencing the expression of said "structural gene" from a distance.

At Claim 1, line 5, and throughout the claims, "promote expression of" is indefinite. It is unclear what is meant by promote. Use of the more definite term --express-- is suggested.

At Claim 2, it is unclear whether the 70% sequence has promoter activity.

At Claim 2, line 2, "homology" is indefinite. The term "homology" is used to define cladistic or evolutionary relationships that go beyond the one to one correspondence of identical nucleotides at identical positions when comparing polynucleotides. "Homology" should be changed to --sequence identity--.

At Claim 3, lines 2-3, "the nucleic acid fragment" is indefinite. It is not clear to which fragment "the nucleic acid fragment" refers, "The nucleic acid fragment" should be --the nucleic acid fragment of SEQ ID NO: 1--.

At Claim 3, line 3, "stringent conditions" is indefinite. It is unclear whether hybridization conditions are low, moderate, or high stringency.

At Claim 4, lines 1-2, "which has the nucleotide sequence shown in SEQ ID NO: 1 in the Sequence Listing" is indefinite. The nucleotide sequence of Claim 1 embraces more than the polynucleotide of SEQ ID NO: 1 or a part thereof. The limitation of does not indicate that the substitutions, deletion, insertion, or additions recited in Claim 1 are to be included.

At Claim 8, "a site upstream of said structural gene" is indefinite. It is not clear how far upstream "a site upstream of said structural gene" is located.

Claim 8 is an incomplete method claim because it does not result in promoting expression of a structural gene. It is also missing an expression step.

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: wherein expression of said structural gene is increased.

At Claim 9, line 2, "character" is indefinite. It is not clear whether a morphological, biochemical, genetic, or developmental character is contemplated.

Claim 9 is unclear whether both the claimed plant and progeny retain "the character".

Claim 9 recites the limitation "the character" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-9 rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The DNA of Claim 1, since it has not been isolated by the hand of man reads as a product of nature, thus falling outside the five classes of patentable subject matter. The DNA molecule, as claimed, has the same characteristics and utility as those found naturally in the genome or as cellular precursors thereof and therefore does not constitute patentable subject matter. See *American Wood v. Fiber Distintegrating Co.*, 90 U.S. 566 (1974), *American Fruit Growers v. Brogdex Co.*, 283 U.S. 2 (1931), *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 33 U.S. 127 (1948), *Diamond v. Chakrabarty*, 206 USPQ 193 (1980).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Ueki J. *et al.*, Plant Cell and Physiology, June 1999; Vol. 40, No. 6; pp. 618-623.

The claims are broadly drawn to a nucleic acid fragment of SEQ ID NO: 1 wherein one or more nucleotides have been either substituted or deleted or wherein one or more nucleotides have been inserted therein or added thereto; a polynucleotide that hybridizes to a polynucleotide of SEQ ID NO: 1 under conditions of unspecified stringency; and a polynucleotide having 70% sequence identity to SEQ ID NO: 1, and drives expression of a structural gene, and a method thereof.

Ueki teaches the first intron of the rice PDL gene (i.e. a nucleic acid fragment of SEQ ID NO: 1 wherein one or more nucleotides have been either substituted or deleted or wherein one or more nucleotides have been inserted therein or added thereto; or a polynucleotide that hybridizes to a polynucleotide of SEQ ID NO: 1 under conditions of unspecified stringency) increasing the expression of GUS, a downstream structural gene, in transformed rice cells on page 619 column 2, first paragraph of Results and in Figure2A on page 620 column 2. The reference teaches all the limitations of Claims 1-8.

All Claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (703) 305-5417. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Russell Kallis Ph.D.
June 2, 2003

PHUONG T. BUI
PRIMARY EXAMINER